Animal Model of Viral Oncogenesis

ELECTRON microscopy showed a virus in the tissues of a strain of guinea-pigs in which leukaemia arose spontaneously. This strain of guinea-pigs dates back to 1906 when inbreeding began at the Bureau of Animal Industry of the US Department of Agriculture[1]. We are at present using one of these families, now known as strain No. 2, in our research. In 1940, these animals were transferred to the National Cancer Institute where inbreeding of this strain has continued until now. A high degree of genetic homogenicity has resulted from this method of breeding. In 1954, Congdon and Lorenz reported several forms of acute lymphatic leukaemia[2]. Ten transplantable tumours were found, and of these four were carried and three were subsequently lost.

Electron microscopy of animals carrying this transmissible leukaemia has revealed a new virus. The leukaemia is at present being transmitted with cell-free leukaemic material, such as plasma or tissue extracts, prepared by repeated ultracentrifugation at speeds up to 40,000 r.p.m. The infective agent crosses the placental barrier in the leukaemic mother and has been recovered from the gastrointestinal and urinary tracts. Feeding leukaemic spleen cells has also produced the disease. Lines of guinea-pigs other than strain No. 2 are almost entirely resistant; but the disease can be serially propagated, with a 100 per cent mortality rate, in F_1 hybrids originating from crossmating susceptible strain No. 2 animals with resistant Hartley guinea-pigs. F_1 hybrids, irrespective of age, are now used exclusively. After injection by various routes, the disease has an average incubation period of 18 days and ends in death with blast cell counts in the peripheral blood up to 350,000 cells/mm^3. Autopsy shows widespread leukaemic involvement of the entire haematopoietic apparatus[3]. The leukaemia is of special interest because the experimental disease resembles the human disease very closely in its haematological and pathological responses. Tissues from animals in the terminal stages of acute leukaemia were examined with light and electron microscopes. Viral particles could readily be demonstrated in plasma pellets, lymphoid tissue and megakaryocytes in all animals examined[4]. Control animals had no particles.

The guinea-pig leukaemia virus is about 85 mμ in diameter. It resembles the type *C* particles associated with murine leukaemia but differs in detail. The virus is smaller and the intermediate layer is not as electron dense (Fig. 1). The virus particles can be seen to bud into the cisterna of the endoplasmic reticulum (Fig. 2). The particles were present in high-speed plasma pellets, bone marrow, spleen and lymph node biopsies when the guinea-pigs had peripheral white counts of more than 100,000 cells/mm^3 (ref. 5). Light microscope examination showed that almost all organs had been infiltrated by neoplastic lymphoblasts. This virus is destroyed by exposure to ultra-violet light or X-rays, by heating for 30 min at 56° C, by shaking with ether or acetone and by formalinization. The virus is resistant to trypsin. The infectivity of leukaemic spleen cell suspensions treated with glycerine and calf serum can be preserved by storing them at −90° C for up to 5 months.

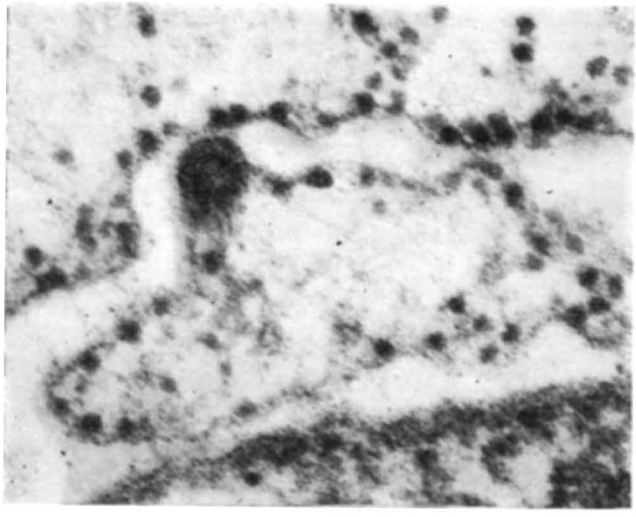

Fig. 1. Section of part of a cell from the bone marrow of a leukaemic guinea-pig. The particle can be seen budding from membranes of the endoplasmic reticulum. (×*c.* 142,500.)

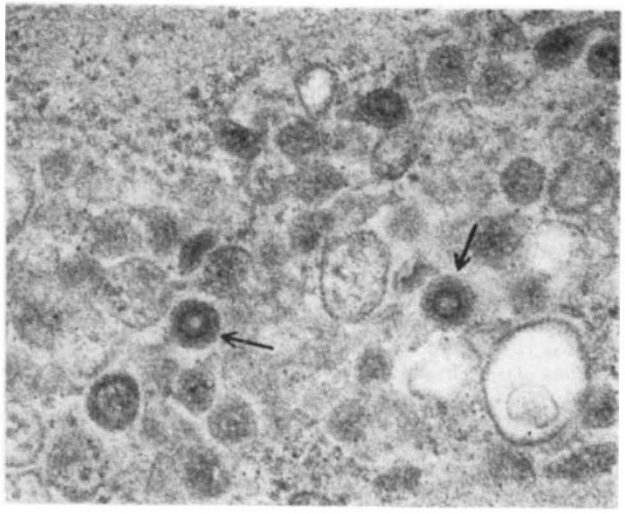

Fig. 2. Particles present in a plasma pellet from a leukaemic guinea-pig. (×*c.* 86,700.)

Leukaemia in guinea-pigs appears to be limited to this strain and associated with the presence of viral particles. Virus recovered from the blood of guinea-pigs with induced leukaemia, using resuspended pellets obtained by ultracentrifugation, has induced leukaemia when injected into susceptible guinea-pigs. We have found that the virus acts as a potent antigen in homologous host species. It seems that a new animal model system for work in viral oncogenesis has been opened up by the demonstration of a new viral leukaemia in a strain of inbred guinea-pigs.

STANLEY R. OPLER

Department of Pathology,
Columbia University,
Lenox Hill Hospital,
New York.

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[1] Heston, W. E., and Deringer, M. K., *J. Nat. Cancer Inst.*, **13**, 705 (1952).
[2] Congdon, C. C., and Lorenz, E., *Amer. J. Pathol.*, **30**, 337 (1954).
[3] Opler, S. R., *Sixth Intern. Cong. I.A.P.*, Kyoto, October (1967).
[4] Opler, S. R., *Sci. Proc. Amer. Assoc. Pathol. and Bact.*, March (1967).
[5] Opler, S. R., *Proc. Amer. Assoc. Cancer Res.*, March (1967).

Recognition of the Individuality of Tumour Strain by Sensitized Peritoneal Lymphoid Cells

Odashima[1] and Yoshida[2] have demonstrated the biological individuality of more than fifty different strains of rat ascites hepatomata. Even in strains originating from the same animal, there are marked differences in the pattern of growth as well as differences in such cytological characters as chromosome constitution or sensitivity to antitumour agents[3]. Antigenic differences among these strains have not, however, been investigated.

Over the past 2 years, four different strains of ascites hepatoma, *AH-64A*, *AH-64B*, *AH-64C* and *AH-64D*, and six sub-strains have been established, all of which originated from primary tumour ascites or separate hepa-